

IMMUNOTHERAPY FOR THE TREATMENT OF LUNG CANCER

A guide for patients and caregivers



free to breathe
a partnership for lung cancer survival

FREE TO BREATHE
SUPPORT LINE
(844) 835-4325

A FREE resource for lung
cancer patients
& caregivers

About this brochure

Immunotherapy is a new and exciting way to treat lung cancer. Immunotherapy works differently than other lung cancer treatments, such as chemotherapy. This brochure helps explain how immunotherapy works and what side effects can happen with immunotherapy.

Keep in mind that immunotherapy is not an option for every patient with lung cancer. Your doctor can recommend options to treat your *specific* lung cancer. A list of questions to ask your doctor is included at the end of this brochure. We hope that this brochure is useful to you in helping you understand immunotherapy.

The information in this brochure is not intended to be a substitute for medical advice provided by your healthcare team.

We encourage you to speak with your doctor or nurse about your specific lung cancer, tests and treatments.

About Free to Breathe

We are Free to Breathe. We are a partnership of lung cancer survivors, advocates, researchers, healthcare providers and industry leaders. We are united in the belief that every person with lung cancer deserves a cure.

For additional patient resources, please visit freetobreathe.org.



What is immunotherapy?

Immunotherapy is a way to treat lung cancer that is different from chemotherapy or targeted therapies. Immunotherapies are designed to make use of your body's own immune system to fight cancer.

What immunotherapies are available?

A number of immunotherapies have been approved to treat patients with lung cancer in different settings. Please see the **Immunotherapy Quick Guide** at the back of this brochure for a listing of the immunotherapy drugs that are currently approved. Many other

immunotherapies are being studied and could be approved by the FDA.

Keep in mind that immunotherapy for lung cancer is still relatively new. More research is being done to help understand which people are most likely to benefit from immunotherapy and how best to use these treatments. **Ask your doctor if an immunotherapy might be an option for you.**

How is immunotherapy given?

Immunotherapies are given through a vein (usually in your arm), but differ in how often they are given.

What is the immune system and how does it work?

The immune system is your body's defense against disease. Your immune system can recognize and destroy infections (such as

The immune system has the ability to recognize things that do not belong in the body, such as bacteria, viruses or cancer cells.

bacteria and viruses) and abnormal cells (such as cancer cells).

Many specialized cells, tissues, and organs of your immune system work together to defend your body against foreign invaders and abnormal cells. The frontline of your immune system includes cells in your bloodstream called white blood cells. Different types of white blood cells can recognize and attack foreign substances (eg, bacteria or viruses) or abnormal cells in different ways.

T-cells are a type of white blood cell that can recognize when a cell is infected or if it is

How the immune system normally works to fight cancer

Figure 1A: T-cells recognize the cancer cell as something that is not supposed to be there.

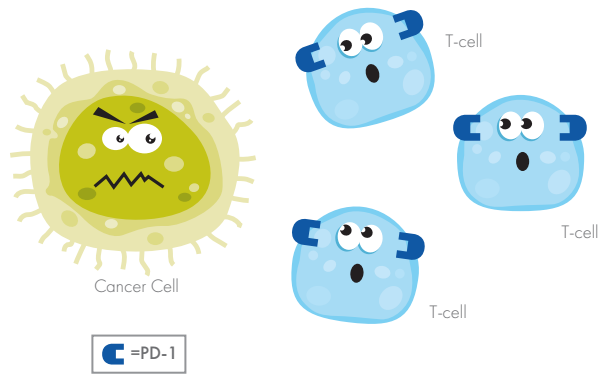
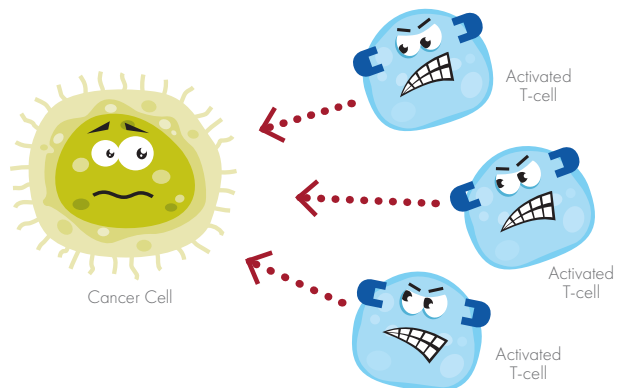


Figure 1B: T-cells then become activated to help destroy the cancer cell.



abnormal, such as a cancer cell. Once T-cells recognize that a cell is infected or is cancer, T-cells are activated and work to destroy the abnormal cell (Figure 1).

How do cancer cells avoid the immune system?

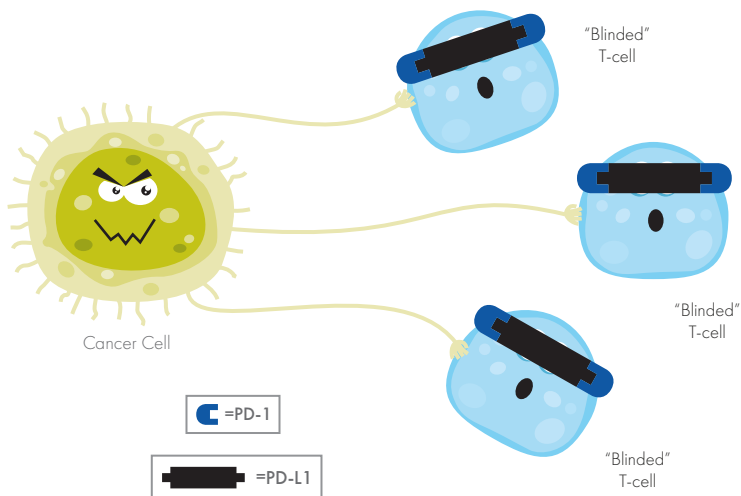
Sometimes cancer cells find ways to trick the immune system into thinking that they are normal and should not be attacked. One way this happens is through proteins on cells called checkpoint proteins. PD-L1 and PD-1 are types of checkpoint proteins. PD-L1 is found on many

types of normal, healthy cells. PD-1 is often found on T-cells.

Sometimes cancer cells escape the immune system by making their own PD-L1. When cancer cells make their own PD-L1, it can bind to PD-1 on T-cells. The end result is that T-cells no longer recognize that the cancer cell is abnormal (Figure 2). In other words, the cancer cells become “invisible” to T-cells. The T-cells no longer attack the cancer and the cancer cells are allowed to continue to grow and spread.

Making PD-L1 is one way that cancer cells “hide” from the immune system

Figure 2. When cancer cells make their own PD-L1, T-cells don’t “see” the cancer cells.



How do the available immunotherapies work?

Scientists have been developing new ways to activate the immune system to attack cancer cells. One strategy is to prevent cancer cells from making themselves invisible. Checkpoint inhibitors are a type of immunotherapy that use this strategy.

Some checkpoint inhibitors work by binding to the PD-1 on T-cells. These drugs stop PD-1 from binding to the PD-L1 on cancer cells. When this happens, the cancer cell can no longer trick the immune system (Figure 3A).

Other checkpoint inhibitors work by binding to PD-L1 instead of PD-1 (Figure 3B). But, blocking either PD-1 or PD-L1 has the same result: PD-L1 and PD-1 can no longer bind to each other, allowing the T-cells to recognize the tumor cells and destroy them.

Should my tumor be tested for PD-L1?

PD-L1 testing looks at how much PD-L1 is found in your tumor. Testing is done by taking a small sample of your tumor (a biopsy), which is sent to a lab. Some studies suggest that the more PD-L1 a tumor has, the more likely the patient will respond to an immunotherapy. But, studies have also shown that not everyone

with high PD-L1 levels will respond to immunotherapy. Scientists are working to better understand which patients are most likely to benefit from immunotherapy.

Your doctor may recommend testing your tumor to see how much PD-L1 is in your tumor.

How is immunotherapy monitored?

Your doctor will likely recommend scans to see how your tumor is responding to the immunotherapy.

Immunotherapies work differently from chemotherapy. When a patient is treated with chemotherapy, changes in the size of a tumor can be measured quickly on a CT scan—often within days. With immunotherapy, the benefits can take much longer to appear.* Researchers aren't exactly sure why this happens, but it may be because the immune response takes a little while to become fully active.

*Sometimes, immunotherapy causes T-cells and other immune cells to flock to the tumor, making it appear to get larger before it begins to shrink (pseudoprogression).

Your doctor will work with you to determine how to best monitor your progress while you are on an immunotherapy.

With immunotherapy, the good guys win

Figure 3A. Some immunotherapy drugs bind to PD-1 so that it can't interact with PD-L1.

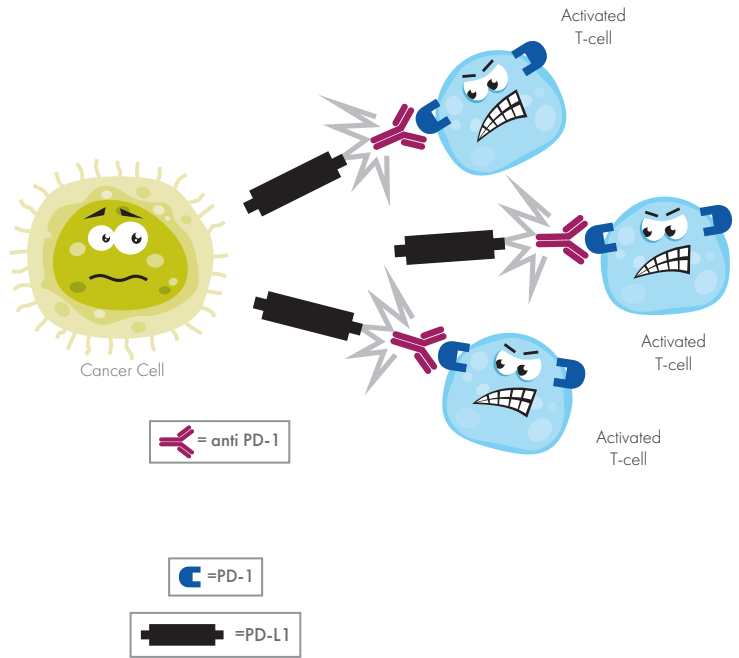
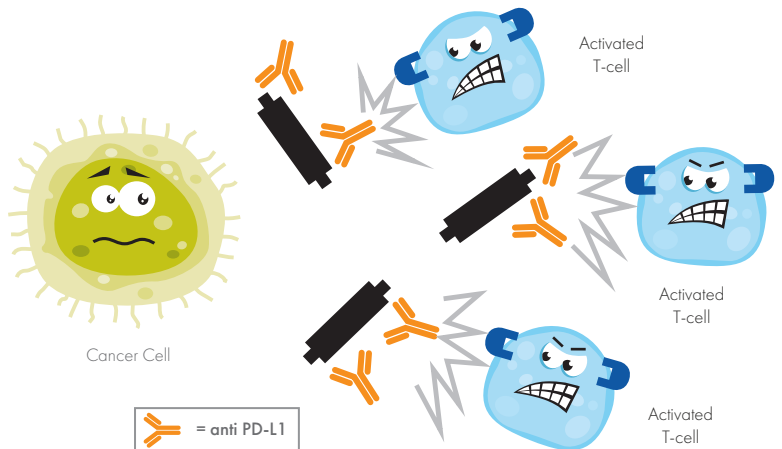


Figure 3B. Other immunotherapies bind to PD-L1 and stop PD-L1 from binding to PD-1. The end result is that T-cells can recognize and destroy the cancer cell.



What are the side effects of immunotherapy?

Immunotherapy works differently than other cancer treatments, such as chemotherapy. The side effects of immunotherapy are also different from those of other types of treatments.

Immunotherapy can cause many different types of side effects, which can happen at any time. Common side effects of immunotherapy are generally mild and can include feeling tired (fatigue), itching, skin rashes, muscle, joint or bone pain, and nausea.

But, immunotherapy can sometimes cause your immune system to become too active. This may cause your body to react against normal tissues, such as your lungs, liver, colon, or thyroid (see Table). This can be a particular concern in patients who have had an organ transplant or who already have immune system problems such as Crohn's disease, ulcerative colitis, or lupus. You should discuss with your doctor if you have experienced any of these before starting an immunotherapy.








If your immune system overreacts, conditions such as pneumonitis (a lung problem with symptoms of cough, chest pain, or shortness of breath), or colitis (an intestinal problem that can cause diarrhea), can occur. **Getting help from your doctor right away may help keep these problems from becoming more serious.**

Side effects of immunotherapy are treated differently than those of chemotherapy. Depending on the side effects, your immunotherapy could be stopped. You may also be given steroid treatment for your side effects. Be sure to talk to your doctor about any concerns or side effects that you experience.

If you become ill when you are away from your own doctor or hospital, you should let the doctor treating you know that you are on an immunotherapy.

Be sure to let your doctor know right away if you have new symptoms or if existing symptoms get worse.

Possible side effects of immunotherapy

Part of the body	Possible side effects	What you may feel
 <p>Lungs</p>	<p>Inflammation of the lungs (pneumonitis)</p>	<ul style="list-style-type: none"> • Shortness of breath • Cough • Chest pain
 <p>Intestine</p>	<p>Inflammation of the colon (colitis)</p>	<ul style="list-style-type: none"> • Diarrhea • Pain in the stomach area
 <p>Liver</p>	<p>Inflammation of the liver (hepatitis)</p>	<ul style="list-style-type: none"> • Dark urine • Feeling less hungry
 <p>Thyroid or other hormone glands</p>	<p>Thyroid problems, such as underactive thyroid (hypothyroidism)</p>	<ul style="list-style-type: none"> • Feeling cold • Headaches • Weight loss or gain
 <p>Kidney</p>	<p>Inflammation of the kidney (nephritis)</p>	<ul style="list-style-type: none"> • Change in the amount or color of your urine
 <p>Infusion reactions</p>	<p>Side effects related to IV administration</p>	<ul style="list-style-type: none"> • Chills • Fever • Rash or itching
 <p>Skin or other organs</p>	<p>Rash, eye problems, or muscle problems</p>	<ul style="list-style-type: none"> • Rash • Changes in eyesight • Muscle pain or weakness

These are not all the possible side effects of immunotherapy.

Questions you may want to ask your doctor

What are the options for treating my lung cancer?

- Surgery?
- Radiation?
- Chemotherapy?
- Immunotherapy?
- Targeted therapy?
- Clinical trial?

Has my tumor been tested for mutations (eg, EGFR, ALK, ROS1) or other biomarkers?

- If not, why not?
 - If not, would a blood test to check for mutations be right for me?
- If yes, what were the results?
 - If I do not have a mutation, would immunotherapy or chemotherapy be an option for me?
 - If I have a mutation, would targeted therapy be an option for me?

Has my tumor been tested for PD-L1?

- If not, why not?
- If yes, is immunotherapy an option for me?

Where will I receive my treatment?

- In a hospital?
- In a doctor's office or clinic?

What are the main side effects of my treatments?

What supportive care (or palliative) treatments are available to me?

What is my overall treatment plan?

- If this is my first treatment, what might be the next treatment?
- If this is my second treatment, how is it different from my first treatment?



The Free to Breathe Support Line provides education, connection to resources and opportunities for meaningful engagement. We strive to help patients and caregivers better face the challenges of lung cancer. Free to Breathe is committed to building and empowering the lung cancer community.

We are available Monday through Friday
between 8 am and 4 pm Central Time, toll free:
[\(844\) 835-4325](tel:(844)835-4325)

Patients and caregivers may call as often as they wish,
and the service is offered completely free of charge!

You may also contact us at: support@freetobreathe.org

Join our online community at: healthunlocked.com/freetobreathe

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we are
FREE TO BREATHE

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IMMUNOTHERAPY FOR TREATMENT OF LUNG CANCER: A QUICK GUIDE

As of July 2017, the FDA has approved three immunotherapy drugs for the treatment of metastatic non-small cell lung cancer (NSCLC):

- Nivolumab (Opdivo®)
- Pembrolizumab (Keytruda®)
- Atezolizumab (Tecentriq®)

Nivolumab and pembrolizumab are PD-1 inhibitors (they bind to PD-1), whereas atezolizumab is a PD-L1 inhibitor. Regardless, they all work to stop PD-1 and PD-L1 from binding together. The end result is that T-cells can “see” the tumor cells and the immune system works to destroy the cancer.

The FDA has approved different drugs for different situations (see Table on the back of this guide). More immunotherapies are likely to be approved within the next few months.

Pembrolizumab is approved as first line (initial) therapy for patients with advanced NSCLC who have not been treated with chemotherapy or targeted therapy. Pembrolizumab by itself is used to treat patients whose tumors have high levels (50% or more) of a protein called PD-L1 and no EGFR or ALK mutations. See pages 5-7 of the immunotherapy booklet to learn more about PD-L1.

Pembrolizumab in combination with two chemotherapy drugs (pemetrexed and carboplatin) is also approved for first-line treatment of patients with advanced, non-squamous NSCLC. This combination of pembrolizumab and chemotherapy may be used regardless of the amount of PD-L1 in the tumor.

All three immunotherapies (nivolumab, pembrolizumab and atezolizumab) are approved to treat patients with NSCLC whose tumor progresses (gets worse) after chemotherapy or targeted therapy. When used after chemotherapy stops working:

- Pembrolizumab is approved for patients whose tumors have at least some PD-L1
- Nivolumab and atezolizumab are approved regardless of whether the tumor has any PD-L1

Please visit freetobreathe.org for more information on lung cancer and treatments.

Type	Drug	Use when newly diagnosed??	Use in combination with chemotherapy?	Use after chemotherapy stops working?	Requires PD-L1 testing?
PD-1 inhibitor	Nivolumab (Opdivo)	N	N	Y	N
	Pembrolizumab (Keytruda)	Y	Y*	Y	N (when used in combination with chemotherapy)* Y (when used by itself for initial therapy or after chemotherapy stops working)
PD-L1 inhibitor	Atezolizumab (Tecentriaq)	N	N	Y	N

*Pembrolizumab is approved in combination with chemotherapy (pemetrexed and carboplatin) in patients with non-squamous NSCLC

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